REMARKS

Claims 1-35 were pending in the present application. Claims 14-26 and 35 have been cancelled, without prejudice, as being directed to a non-elected invention. Claim 31 has also been cancelled without prejudice and claims 1-3, 5-12, 27, 32 and 34 have been amended. Accordingly, claims 1-13, 27-30 and 32-34 will remain pending, after the amendments presented herein have been entered.

Support for the amendments to the claims may be found throughout the specification including the originally filed claims. In particular, support for the amendments to claims 6 and 27 may be found at, for example, page 4, line 28 through page 5, line 2 of the specification. Support for the addition of SEQ ID NO:6 in Table 1 may be found in the parent application (serial no. 09/643260) in Table 1 (see page 46 of the parent specification).

A substitute paper copy as well as a computer-readable form of the sequence listing is also being submitted herewith. The content of the substitute paper and computer readable copies of the sequence listing are the same and include no new matter, as required by 37 C.F.R. §§1.825(a) and (b)

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 1-4, 6-13 and 27-34 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-4, 6-13 and 27-34 under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that

> [c]laims 1,2, 10, 11, 27, 31, 32 and 34 are indefinite because of the use of the term "NEMO". An acronym/abbreviation should be preceded by the full spelled out word. Claims 4 and 13 are included in the rejection because they are

> dependent on rejected claims and do not correct the deficiency of the claim from which they depend. Claims 2, 3, 11, 12, 27 and 31 are indefinite because of the use of the term "IKK." An acronym/abbreviation should be preceded by the full spelled out word. Claims 2, 7, 8, 9, 11 and 31 are indefinite because of the use of the term "capable." It is not clear whether the anti-inflammatory compound actually blocks... (claim 2, 11,31) and capable of inhibiting... (claim 7, 9) and capable of down-regulating... (claim 8), or merely have the capability to do so. The word capable associates with the latent function only. Claim[s] 6 and 27 [are] indefinite because they lack essential steps as claimed in the method of treatment of inflammatory disorder or treating an NFkB-mediated condition in a subject. The omitted steps are: the site and method of administration, and a step whereby the desired outcome and the time for the effective treatment using anti-inflammatory compound can be determined. Claims 7-9 and 28-34 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

With respect to claims 1,2, 3, 7, 8, 9, 10, 11, 12, 27, 32 and 34, Applicants respectfully submit that, while in no way acquiescing to the validity of the Examiner's rejections, Applicants have amended the claims thereby rendering the foregoing rejections moot. Specifically, claims 1,2, 5, 10, 11, 27, 32 and 34 have been amended such that the acronym "NEMO" is spelled out in the claims; claims 2, 3, 11, 12 and 27 have been amended such that the acronym "IKK" is spelled out in the claims; and claims 2, 7, 8, 9 and 11 have been amended such that they no longer recite the phrase "capable of."

With respect to claims 6 and 27, Applicants respectfully traverse the foregoing rejection on the grounds that claims 6 and 27 are clear and definite and would be understood by one of skill in the art as required by 35 U.S.C. §112, second paragraph. Claim 6, and claims depending therefrom, are directed to methods for treating a subject suffering from an inflammatory disorder by administering to the subject an anti-inflammatory compound comprising at least one NF-κB Essential Modulator (NEMO) binding domain in an amount and for a period of time effective to block the recruitment of leukocytes into sites of inflammation, thereby treating the subject suffering from an inflammatory disorder. Claim 27, and claims depending therefrom, are directed to methods for treating an NFkB-mediated condition in a subject by administering to the subject an anti-inflammatory compound comprising at least one NF-κB Essential Modulator (NEMO) binding domain in an amount and for a period of time effective to inhibit the binding of

NF-κB Essential Modulator (NEMO) to an IκB protein kinase (IKK), thereby treating an NFkB-mediated condition in a subject.

Contrary to the Examiner's assertions, the claims need not specify the site and method of administration of the anti-inflammatory compound. Such a requirement would unduly limit the scope of the claims since, as taught in Applicants' specification multiple sites and methods of administration would be appropriate for the methods of the invention (see, for example, the teachings at pages 26-30 of the specification). Applicants would like to respectfully remind the Examiner that, as indicated by M.P.E.P. § 2173.04, the breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, then the claims comply with the requirements of 35 U.S.C. §112, second paragraph. In fact, as indicated by M.P.E.P. § 2173.05(c),

> recent cases have tended to accept a limitation such as "an effective amount" as being definite when read in light of the supporting disclosure and in the absence of any prior art which would give rise to uncertainty about the scope of the claim. In *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected.

Similarly, in the present case Applicants' specification provides ample guidance with respect to the amount of an anti-inflammatory compound which is effective in the methods of the invention and with respect to modes and time frames of administration of the anti-inflammatory compounds that are suitable for the claimed methods (see, for example, pages 26-30 of the specification and Examples 8-10). For instance, in Example 8 Applicants describe the treatment of two distinct animal models of acute inflammation using the anti-inflammatory compounds of the invention. This example describes the successful administration of an anti-inflammatory compound both topically (in the ear of animals suffering from ear edema) and systemically (in animal models of peritonitis). In view of the foregoing, it is evident that, when read in light of the supporting disclosure, claims 6 and 27 are clear and definite and comply with the

requirements of 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 1, 5, 27, 32 and 34 Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 5, 27, 32 and 34 under 35 U.S.C. §102(b) as anticipated by Houston *et al.* (US 5,166,133). The Examiner relies on Houston *et al.* for teaching "a method for inhibiting adhesion of white blood cells to endothelial cells to prevent inflammatory type diseases by administering proteins selected from inter-alpha-trypsin inhibitor, alpha i-M and HI-30 (see abstract, summary of the invention, SEQ ID NO: 17, col 27), wherein the peptide derived from alphal-M has 100% sequence identity to SEQ ID NO: 6 (see sequence alignment result. IssuedJPatents_AA database, Accession NO: US-07-700-526-17, August 16, 1991)." In particular, the Examiner is of the opinion that

> Houston's peptide is considered identical to the anti-inflammatory compound of method claims 1, 5 and 27, 32 and 34 of [the] instant application. Since Houston's protein is considered identical to anti-inflammatory compound of method claims 1, 5 and 27, 32 and 34, therefore the sequence of this protein is considered to have the NEMO binding domain of the claimed anti-inflammatory compound, and also contacting a cell with an effective amount of this sequence would have been modulated [*sic*] the NF-kB induction in that cell, thus, anticipating claims 1, 5, 27, 32 and 34.

Applicants respectfully traverse the foregoing rejection for the following reasons.

Claim 1, and claims depending therefrom, are directed to methods for modulating NF-κB induction in a cell comprising contacting a cell with an effective amount of an anti-inflammatory compound comprising at least one NF-κB Essential Modulator (NEMO) binding domain, thereby modulating NF-κB induction in a cell. Claim 27, and claims depending therefrom, are directed to methods for treating an NFkB-mediated condition in a subject, comprising administering to the subject an anti-inflammatory compound comprising at least one NF-κB Essential Modulator (NEMO) binding domain in an amount and for a period of time effective to inhibit the binding of NF-κB Essential Modulator (NEMO) to an IκB protein kinase (IKK), thereby treating an NFkB-mediated condition in a subject.

For a prior art reference to anticipate in terms of 35 U.S.C. §102 a claimed invention, the prior art must teach ***each and every element*** of the claimed invention. Lewmar Marine v. Barient, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

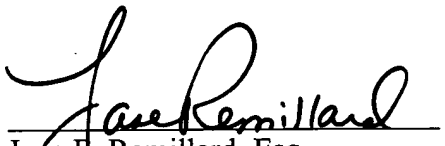
Houston *et al.* disclose proteins such as inter-α-trypsin inhibitor, a1-M and HI-30, which affect the adhesion of white blood cells to endothelial cells (see, for example, the abstract). There is no teaching or suggestion in Houston *et al.* with respect to NF-kB induction, much the less any disclosure on anti-inflammatory compounds comprising fusions of a NEMO binding domain and at least one membrane translocation domain. The Examiner appears to be basing this rejection on an alignment which shows a 100% identity between SEQ ID NO:6 in Applicants' Sequence Listing and SEQ ID NO:17 of Houston *et al.* However, SEQ ID NO:6 is a "nonsense" sequence (Xaa1 Xaa2 Xaa3 Xaa4 Xaa5 Xaa6 Xaa7, with each of Xaa1-7 being defined as being any amino acid) which was introduced into the Sequence Listing in error. A substitute Sequence Listing is provided herewith in which SEQ ID NO:6 has been properly identified. Houston *et al.* do not teach or suggest this sequence.

In view of all of the foregoing, it is evident that Houston *et al.* do not anticipate the pending claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

CONCLUSION

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



Jane E. Remillard, Esq.
Registration Number 38,872
Attorney for Applicants

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400
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